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Alopecia syphilitica, from diagnosis to treatment

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ABSTRACT

Alopecia syphilitica (AS) is an uncommon manifestation of secondary syphilis, with a prevalence that ranges from 3% to 7%. It is a nonscarring alopecia that can present in a diffuse pattern, a moth-eaten pattern, or a mixed subtype. Due to its low prevalence and similar presentation to other forms of alopecia such as alopecia areata, telogen effluvium, and tinea capitis, dermatologists must maintain a high degree of suspicion for prompt diagnosis. The diagnosis of AS is made by eliciting the patient's history, obtaining serologic tests, and examining histopathologic or dermatoscopic findings. First-line treatment includes benzathine penicillin G injection, which leads to hair regrowth weeks to months after administration. In this article, we present a focused review on the diagnosis of AS and discuss evidence-based therapeutic approaches for the management and treatment of this condition.

KEYWORDS Alopecia; alopecia syphilitica; hair loss; secondary syphilis

CME

Target audience: All physicians

Learning objectives: After completing the article, the learner should be able to

1. Describe the clinical and trichoscopic findings of alopecia syphilitica
2. Describe possible methods to diagnose alopecia syphilitica
3. Identify treatments for alopecia syphilitica

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Alopecia syphilitica (AS) is an uncommon manifestation of secondary syphilis, with a prevalence that ranges from 3% to 7%.[1] Due to its infrequent occurrence and subtle presentation that can be mistaken for other causes of alopecia, AS is difficult to diagnose. However, given the recent resurgence of syphilis in high-income countries,[2] it is important for dermatologists to recognize the cutaneous symptoms of syphilis for early and effective treatment. In this article, we present a focused review on the diagnosis of AS and discuss evidence-based approaches for its management.

BACKGROUND

Syphilis is a common sexually transmitted infection caused by the spirochete *Treponema pallidum*. It is more commonly observed in men, who are infected at a ratio of 7:1 compared to women. Secondary syphilis is commonly characterized by systemic symptoms including fever, headache, myalgia, and rash involving the palms and soles. Additionally, wart-like lesions on the genitalia and buccal mucosa known as condyloma lata frequently occur. The potential cutaneous findings of secondary syphilis include nonpruritic, erythematous lesions that can be maculopapular, pustular, or nodular. However, hair loss, known as AS, is another possible rare manifestation of secondary syphilis.[3]

CLINICAL PRESENTATION

Differentiating AS from other causes of alopecia can be challenging; thus, diagnosis of AS is established based on clinical history, physical exam, and dermatoscopic findings. A patient with AS will typically present with a history of syphilis and scattered alopecia without inflammation or desquamation.

According to McCarthy's classification of AS, there are two forms: essential and symptomatic AS.[4] Symptomatic AS presents with both alopecic and syphilitic lesions on the scalp, while essential AS appears as alopecia alone.[4] Essential AS can be further subclassified into a moth-eaten, diffuse, or mixed pattern based on the appearance of the lesions. Moth-eaten AS is the most common manifestation of essential AS and presents with small, irregularly bordered alopecic areas throughout the scalp *(Figure 1)*. It is worth noting that the moth-eaten appearance of alopecia is not exclusive to AS and can be found in alopecia areata (AA), tinea capitis, and trichotillomania as well. Diffuse AS presents with diffuse hair loss with a lack of any concentrated region.[5] Mixed-pattern AS is characterized by a combination of moth-eaten regions on the scalp as well as diffuse hair loss.

When AS is examined dermatoscopically, empty ostia with yellow and black coloration, dilated capillaries, an erythematous background, and decreased hair density are seen.[6,7] A lack of exclamation hair, comma hair, flame hairs, or "v" sign excludes the diagnosis of AA, tinea capitis, and trichotillomania, respectively.[4] In addition, while both AA and AS may present with vellus hairs, the vellus hairs in AA patients are generally observed in the center of the hair loss patch, while in AS they are observed at the periphery.[7]

Histological features of AS include perifollicular lymphocytic infiltrate, increased number of telogen and catagen hair follicles, and follicular hyperkeratosis with follicular plugging.[4] AA can be differentiated from AS by the presence of peribulbar eosinophils.[8] Immunohistochemistry may also show the presence of spirochetes in the hair follicle of a patient with AS, suggesting the pathogenic role of the treponeme in the development of alopecia.[9]

DIAGNOSTIC METHODS

Methods currently used for diagnosis of AS include serological screening, immunohistochemistry, and polymerase chain reaction (PCR). Serological, nontreponemal tests such as Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests diagnose secondary syphilis at 100% sensitivity.[10] When used to screen for syphilis, VDRL and RPR have a high sensitivity; however, false-positives are common due to the cross-reactivity with antigens associated with other conditions, such as infectious mononucleosis, rheumatoid arthritis, lupus, and leprosy. Because false-positives may occur with screening tests, the fluorescent treponemal antibody absorption (FTA-ABS) test serves as a specific, confirmatory test to rule out false-positives.[11,12]

In immunohistochemical detection of syphilis, a purified rabbit IgG highly specific for *T. pallidum* is used.[13] The primary limitation of this technique is cross-reactivity with other spirochete organisms such as *Borrelia*.[10] DNA PCR has a high sensitivity in detecting late-stage syphilis in blood, fluid, and tissue samples.[14] However, because the organisms' DNA is degraded while antigens are preserved, the sensitivity is slightly less than immunohistochemistry.

TREATMENT

The drug of choice to treat all stages of syphilis is benzathine penicillin G. Because AS is a manifestation of secondary syphilis, the treatment follows the same guidelines as for secondary syphilis. Adults are given a single dose of 2.4 million units intramuscularly, while infants and children receive 50,000 units/kg with a limit of 2.4 million units in a single dose.[15] For patients with documented penicillin allergy, alternatives include doxycycline 100 mg orally twice daily for 2 to 4 weeks or tetracycline 500 mg orally four times a day for 2 to 4 weeks.[16] Tetracycline administration involves more frequent dosing and side effects such as nausea, vomiting, and diarrhea; therefore, compliance might be an issue. Limited clinical trials suggest that ceftriaxone 1 to 2 g intramuscularly or intravenously for 10 to 14 days has been effective in treating secondary syphilis.[17] Patients with penicillin allergy who have issues with follow-up or compliance with medications should be desensitized and treated with benzathine penicillin.[15]

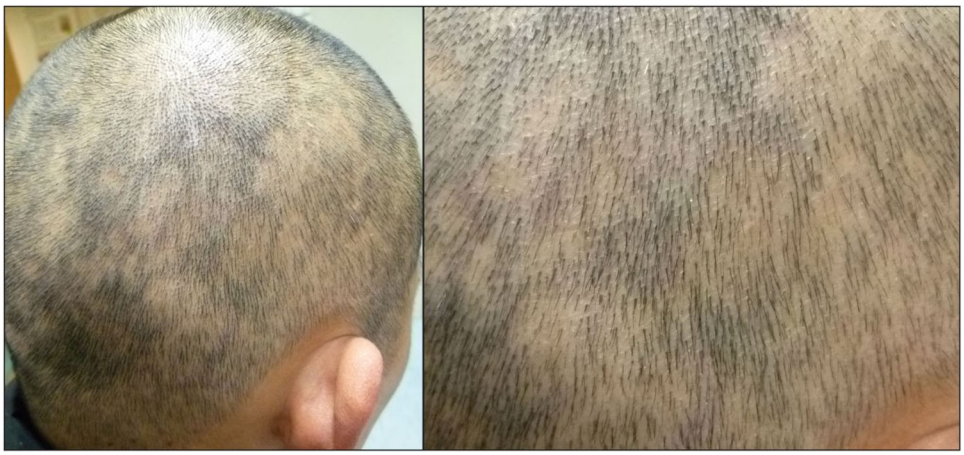

Figure 1. Moth-eaten alopecia syphilitica. Reprinted from Qiao J and Fang H, *CMAJ*,[1] with permission from the Canadian Medical Association.

Pregnant women receive the same treatment as nonpregnant adults, as penicillin is the only known antibiotic that effectively prevents vertical transmission of syphilis.[18] There is currently no treatment alternative to penicillin for pregnant women. When an allergy is present in this population, the patient should be desensitized and treated with benzathine penicillin.[18] Tetracycline antibiotics are contraindicated in pregnancy given the associated teratogenicity. HIV patients with concurrent syphilis who present with AS follow the same treatment guidelines as non–HIV-infected patients in addition to their antiretroviral therapy.

MONITORING RESPONSE TO TREATMENT

The Jarisch-Herxheimer reaction (JHR) is an uncommon but serious possible side effect following antibiotic treatment for syphilis and includes symptoms such as fever, chills, myalgias, arthralgias, and transient headaches within the first 24 hours of treatment. In pregnant women, JHR can induce premature labor or cause fetal distress.[19] Additionally, patients with AS who develop JHR can experience transient hair loss within the 24 hours.[20] While the etiology of this acute febrile reaction is unknown, symptoms require treatment with analgesics, antipyretics, and rest.

After treatment, hair regrowth on the scalp can be expected between 5 and 12 weeks after administration.[4] Clinical monitoring 6 and 12 months after treatment is necessary. However, for HIV patients with AS, monitoring should be more frequent at 3, 6, 9, 12, and 24 months after therapy due to the increased risk of treatment failure in this group. Nontreponemal tests such as VDRL can be used to monitor titers after treatment and should be compared with titers on the day of treatment. If the titer has not decreased over fourfold, then retreatment, serology, and follow-up should be considered. Retreatment for all patients includes weekly injections of benzathine penicillin G 2.4 million units for 3 weeks.[15]

SUMMARY

Due to its low prevalence, AS can be challenging to diagnose and can be mistaken for other leading causes of alopecia such as AA, telogen effluvium, and tinea capitis. Diagnosis is made largely through a thorough evaluation including clinical history, serological testing, and histopathologic and dermatoscopic findings. Dermatoscopic findings of AS include empty ostia, yellow or black dots, dilated capillaries, and decreased hair density. First-line treatment includes benzathine penicillin G intramuscular injection, which leads to hair regrowth weeks to months after administration. Because the medical management of the various types of alopecia varies, it is of great importance for physicians to correctly identify the underlying cause of alopecia in a patient to prevent an increase in the severity and chronicity of the disease.

1. Qiao J, Fang H. Moth-eaten alopecia: a sign of secondary syphilis. *CMAJ*. 2013;185(1):61–61. doi:10.1503/cmaj.120229.
2. Clement ME, Hicks CB. Syphilis on the rise: what went wrong?. *JAMA*. 2016;315(21):2281–2283. doi:10.1001/jama.2016.7073.
3. Webb AN, Langley RGB, Hatchette TF. Answer: can you identify this condition? *Can Fam Physician*. 2012;58(4):410–411.
4. Ye Y, Zhang X, Zhao Y, et al. The clinical and trichoscopic features of syphilitic alopecia. *J Dermatol Case Rep*. 2014;8(3):78–80. doi:10.3315/jdcr.2014.1176.
5. Mysore V, Parthasaradhi A, Kharkar R, et al. Expert consensus on the management of telogen effluvium in India. *Int J Trichol*. 2019;11(3):107–112. doi:10.4103/ijt.ijt_23_19.
6. Errichetti E, Stinco G. Dermoscopy in general dermatology: a practical overview. *Dermatol Ther (Heidelb)*. 2016;6(4):471–507. doi:10.1007/s13555-016-0141-6.
7. Tognetti L, Cinotti E, Perrot J-L, Campoli M, Rubegni P. Syphilitic alopecia: uncommon trichoscopic findings. *Dermatol Pract Concept*. 2017;7(3):55–59. doi:10.5826/dpc.0703a12.
8. Lee JY, Hsu ML. Alopecia syphilitica, a simulator of alopecia areata: histopathology and differential diagnosis. *J Cutan Pathol*. 1991;18(2):87–92. doi:10.1111/j.1600-0560.1991.tb00133.x.
9. Nam-Cha SH, Guhl G, Fernández-Peña P, Fraga J. Alopecia syphilitica with detection of *Treponema pallidum* in the hair follicle. *J Cutan Pathol*. 2007;34(s1):37–40. doi:10.1111/j.1600-0560.2006.00726.x.
10. Carlson JA, Dabiri G, Cribier B, Sell S. The immunopathobiology of syphilis: the manifestations and course of syphilis are determined by the level of delayed-type hypersensitivity. *Am J Dermatopathol*. 2011;33(5):433–460. doi:10.1097/DAD.0b013e3181e8b587.

11. Larsen SA, Steiner BM, Rudolph AH. Laboratory diagnosis and interpretation of tests for syphilis. *Clin Microbiol Rev*. 1995;8(1):1–21. doi:10.1128/CMR.8.1.1-21.1995.
12. Lee WS, Lee MG, Chung KY, Lee JB. Detection of *Treponema pallidum* in tissue: a comparative study of the avidin-biotin-peroxidase complex, indirect immunoperoxidase, FTA-ABS complement techniques and the darkfield method. *Yonsei Med J*. 1991;32(4):335–341. doi:10.3349/ymj.1991.32.4.335.
13. Hoang MP, High WA, Molberg KH. Secondary syphilis: a histologic and immunohistochemical evaluation. *J Cutan Pathol*. 2004;31(9):595–599. doi:10.1111/j.0303-6987.2004.00236.x.
14. Buffet M, Grange PA, Gerhardt P, et al. Diagnosing *Treponema pallidum* in secondary syphilis by PCR and immunohistochemistry. *J Invest Dermatol*. 2007;127(10):2345–2350. doi:10.1038/sj.jid.5700888.
15. Workowski KA, Berman S, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep*. 2010;59(RR-12):1–110.
16. Wong T, Singh AE, De P. Primary syphilis: serological treatment response to doxycycline/tetracycline versus benzathine penicillin. *Am J Med*. 2008;121(10):903–908. doi:10.1016/j.amjmed.2008.04.042.
17. Hook EW, Roddy RE, Handsfield HH. Ceftriaxone therapy for incubating and early syphilis. *J Infect Dis*. 1988;158(4):881–884. doi:10.1093/infdis/158.4.881.
18. Wendel GD, Stark BJ, Jamison RB, Molina RD, Sullivan TJ. Penicillin allergy and desensitization in serious infections during pregnancy. *N Engl J Med*. 1985;312(19):1229–1232. doi:10.1056/NEJM198505093121905.
19. Klein VR, Cox SM, Mitchell MD, Wendel GD. The Jarisch-Herxheimer reaction complicating syphilotherapy in pregnancy. *Obstet Gynecol*. 1990;75(3 Pt 1):375–380.
20. Pareek SS. Syphilitic alopecia and Jarisch-Herxheimer reaction. *Br J Vener Dis*. 1977;53(6):389–390. doi:10.1136/sti.53.6.389.